

HPV Vaccination Update - 2015

Susan Hariri, PhD
Centers for Disease Control and Prevention

May 20, 2015

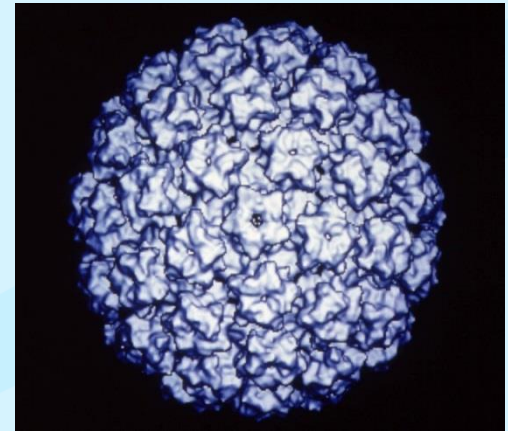
Outline

- ❑ Overview of HPV vaccines
- ❑ HPV-associated cancers due to HPV types
- ❑ Data from 9-valent HPV vaccine trials
- ❑ Updated recommendations of the Advisory Committee on Immunization Practices

Available prophylactic HPV vaccines

- ❑ Virus-like particle (VLP) vaccines
- ❑ The L1 major capsid protein expressed using recombinant technology
- ❑ L1 proteins self-assemble into VLPs
- ❑ Non infectious

HPV VLP



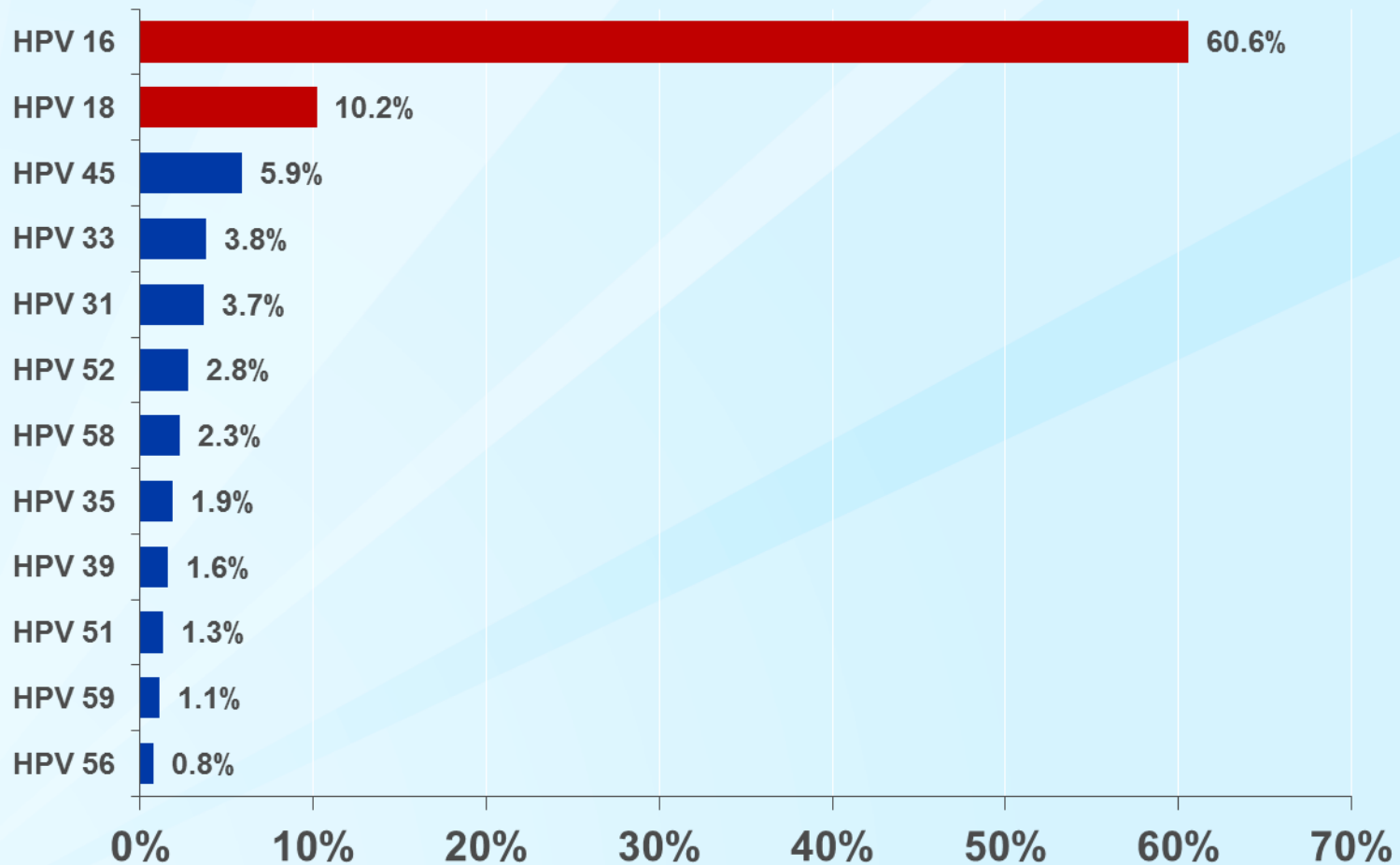
Available HPV vaccines

	Bivalent 2vHPV (Cervarix)	Quadrivalent 4vHPV (Gardasil)
L1 VLP types	16, 18	6, 11, 16, 18
Manufacturer	GlaxoSmithKline	Merck
Adjuvant	AS04: 500 µg aluminum hydroxide 50 µg 3- <i>O</i> -desacyl-4'- monophosphoryl lipid A	AAHS: 225 µg amorphous aluminum hydroxyphosphate sulfate

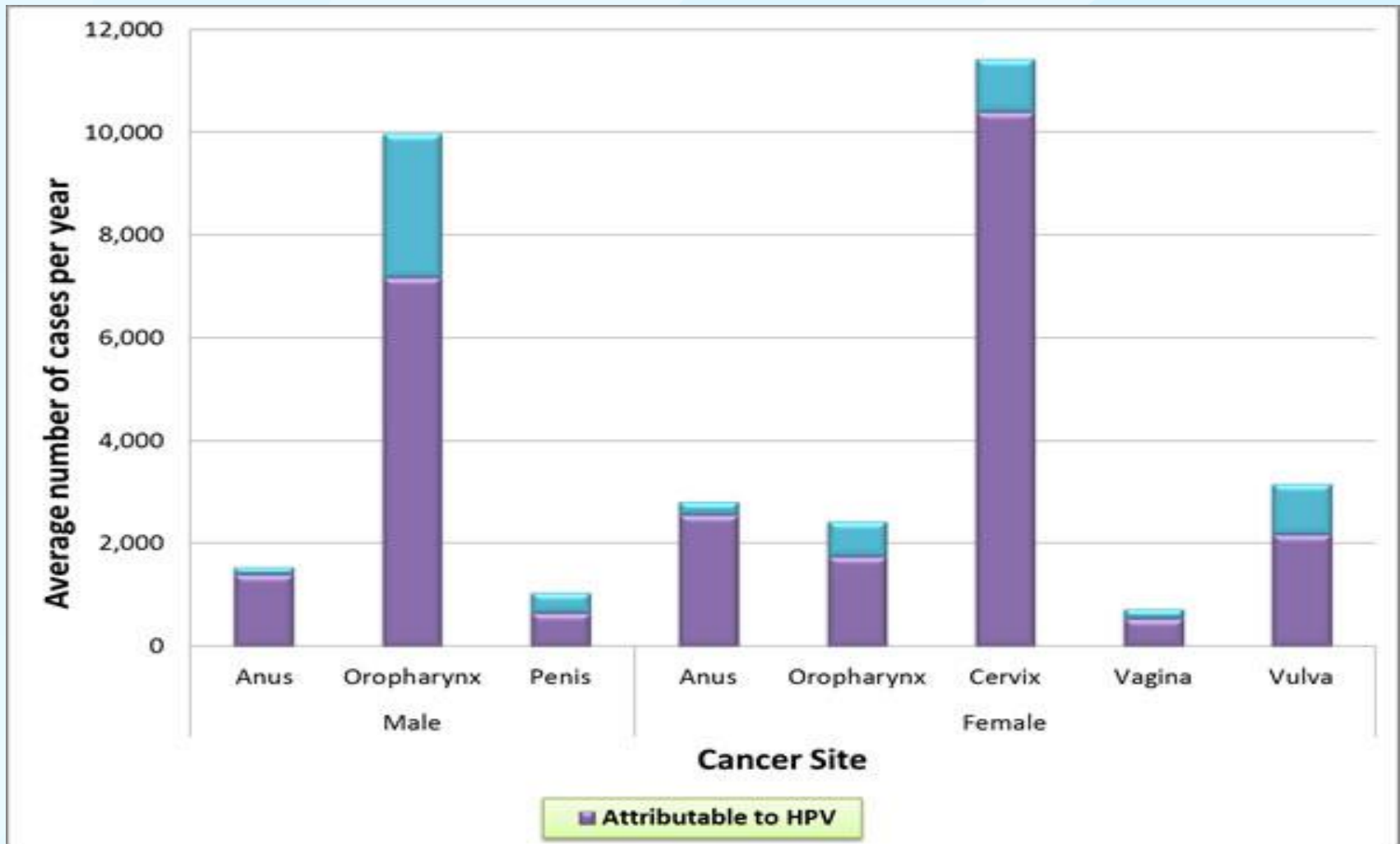
Available HPV vaccines

	Bivalent 2vHPV (Cervarix)	Quadrivalent 4vHPV (Gardasil)	9-valent 9vHPV (Gardasil 9)
L1 VLP types	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45 ,52, 58
Manufacturer	GlaxoSmithKline	Merck	Merck
Adjuvant	AS04: 500 µg aluminum hydroxide 50 µg 3- <i>O</i> -desacyl-4'- monophosphoryl lipid A	AAHS: 225 µg amorphous aluminum hydroxyphosphate sulfate	AAHS: 500 µg amorphous aluminum hydroxyphosphate sulfate

Percentage of cervical cancers attributed to high risk HPV types, worldwide



Estimated number of HPV-attributable cancer cases per year, United States



Estimated percentages of cancers attributed to HPV in the U.S.

Cancer	HPV attributable % (95% CI)	HPV 16/18 attributable % (95% CI)	HPV 31/33/45/52/58 attributable % (95% CI)
Cervical	91 (88-92)	66 (63-69)	15 (12-17)
Vaginal	75 (63-84)	55 (43-67)	18 (11-30)
Vulvar	69 (62-75)	49 (41-56)	14 (10-20)
Penile	63 (52-73)	48 (37-59)	9 (4-17)
Anal			
Male	89 (77-95)	79 (66-88)	4 (1-13)
Female	92 (85-96)	80 (70-87)	11 (6-19)
Oropharyngeal			
Male	72 (68-76)	63 (59-68)	4 (3-7)
Female	63 (55-71)	51 (43-59)	9 (6-15)

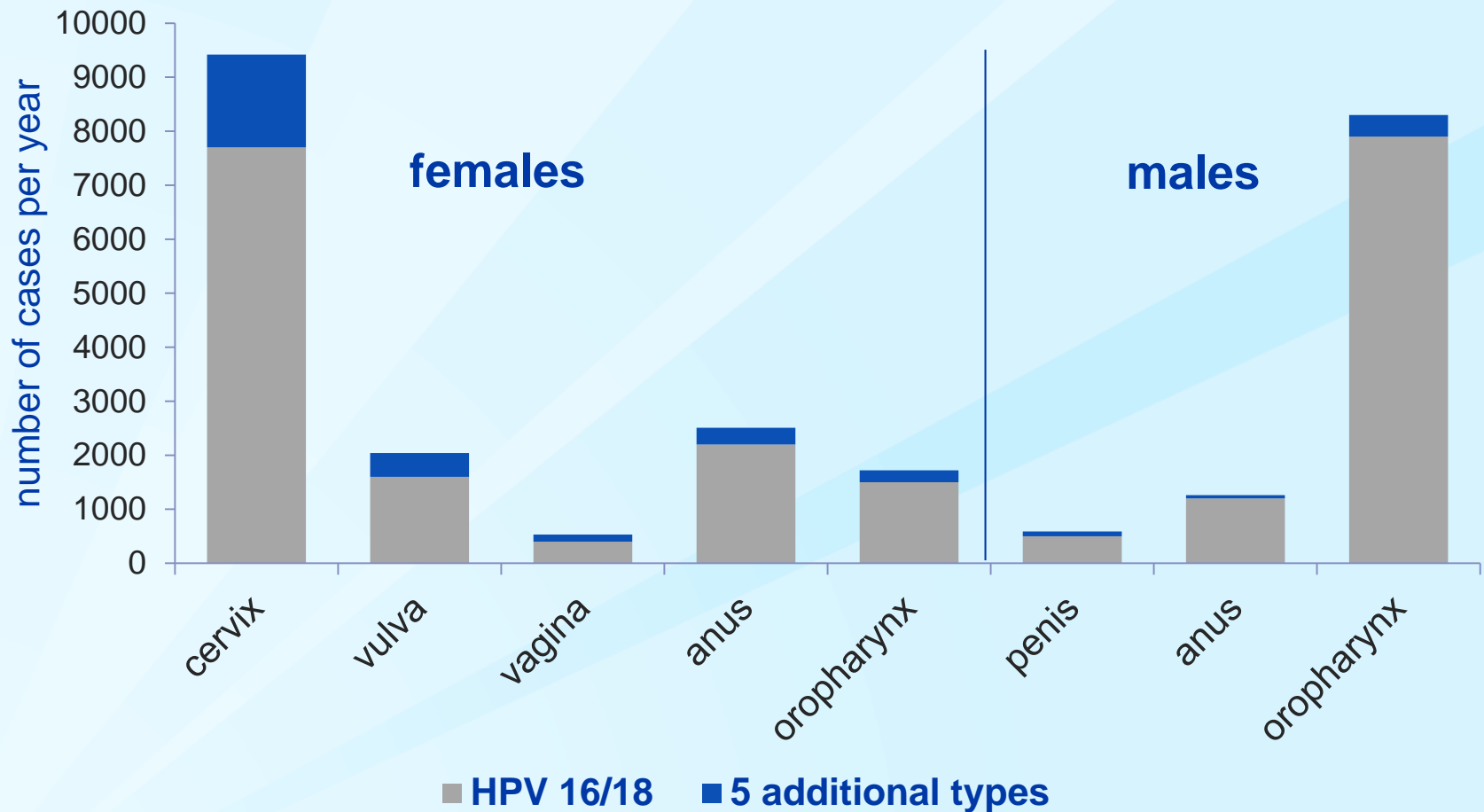
Estimated percentages of cancers attributed to HPV in the U.S.

Cancer	HPV attributable % (95% CI)	HPV 16/18 attributable % (95% CI)	HPV 31/33/45/52/58 attributable % (95% CI)
Cervical	91 (88-92)	66 (63-69)	15 (12-17)
Vaginal	75 (63-84)	55 (43-67)	18 (11-30)
Vulvar	69 (62-75)	49 (41-56)	14 (10-20)
Penile	63 (52-73)	48 (37-59)	9 (4-17)
Anal			
Male	89 (77-95)	79 (66-88)	4 (1-13)
Female	92 (85-96)	80 (70-87)	11 (6-19)
Oropharyngeal			
Male	72 (68-76)	63 (59-68)	4 (3-7)
Female	63 (55-71)	51 (43-59)	9 (6-15)

Estimated percentages of cancers attributed to HPV in the U.S.

Cancer	HPV attributable % (95% CI)	HPV 16/18 attributable % (95% CI)	HPV 31/33/45/52/58 attributable % (95% CI)
Cervical	91 (88-92)	66 (63-69)	15 (12-17)
Vaginal	75 (63-84)	55 (43-67)	18 (11-30)
Vulvar	69 (62-75)	49 (41-56)	14 (10-20)
Penile	63 (52-73)	48 (37-59)	9 (4-17)
Anal			
Male	89 (77-95)	79 (66-88)	4 (1-13)
Female	92 (85-96)	80 (70-87)	11 (6-19)
Oropharyngeal			
Male	72 (68-76)	63 (59-68)	4 (3-7)
Female	63 (55-71)	51 (43-59)	9 (6-15)

Estimated numbers of HPV-associated cancers attributable to HPV 16/18 and 5 additional types in 9-valent vaccine, U.S.*



*Based on years 2006-2010 <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6349a11.htm>
and data from Saraiya, presented at AIN Conference, March 2015

Summary: attribution of HPV 16/18 and HPV 31/33/45/52/58, United States

□ HPV-associated cancers

- ~33,000 per year
- 64% of cancers attributable to HPV 16/18
 - 66% of cervical cancer
 - Other cancers: range, 48% penile -80% anal
- 10% of cancers attributable to additional 5 types
 - 15% of cervical cancer
 - Other cancers: range, 4% oropharyngeal -18% vaginal
 - Differences by sex: 14% for females; 4% for males

□ ≥CIN2 lesions

- ~50% attributable to HPV 16/18
- ~25% attributable to 5 additional types

≥CIN, cervical intraepithelial neoplasia grade 2 or worse
% among all HPV-associated cancers

9-valent HPV vaccine

- ❑ **Licensed by FDA in December 2014**
- ❑ **Clinical development program**
 - Efficacy trial
 - Immunogenicity/immunobridging trials
 - Concomitant use trials

9-valent HPV vaccine efficacy trial

□ Design

- ~14,000 women aged 16-26 years
- Randomized trial: 9vHPV or 4vHPV

□ Objectives

- Demonstrate efficacy for HPV 31,33,45,52,58
- Demonstrate non-inferior immunogenicity for HPV 6,11,16,18

9-valent HPV vaccine efficacy trial per protocol population results

HPV 31,33,45,52,58 related outcomes	9vHPV n/total	4vHPV n/total	Vaccine efficacy (95% CI)
≥CIN2, VIN2/3, VaIN2/3	1/6016	30/6017	96.7 (80.9, 99.8)
6 month persistent infection	35/5939	810/5953	96.0 (94.4, 97.2)

- High efficacy against HPV 31,33,45,52,58 outcomes

≥CIN2 = cervical intraepithelial neoplasia grade 2 or 3, or adenocarcinoma in situ; VIN = vulvar intraepithelial neoplasia; VaIN = vaginal intraepithelial neoplasia

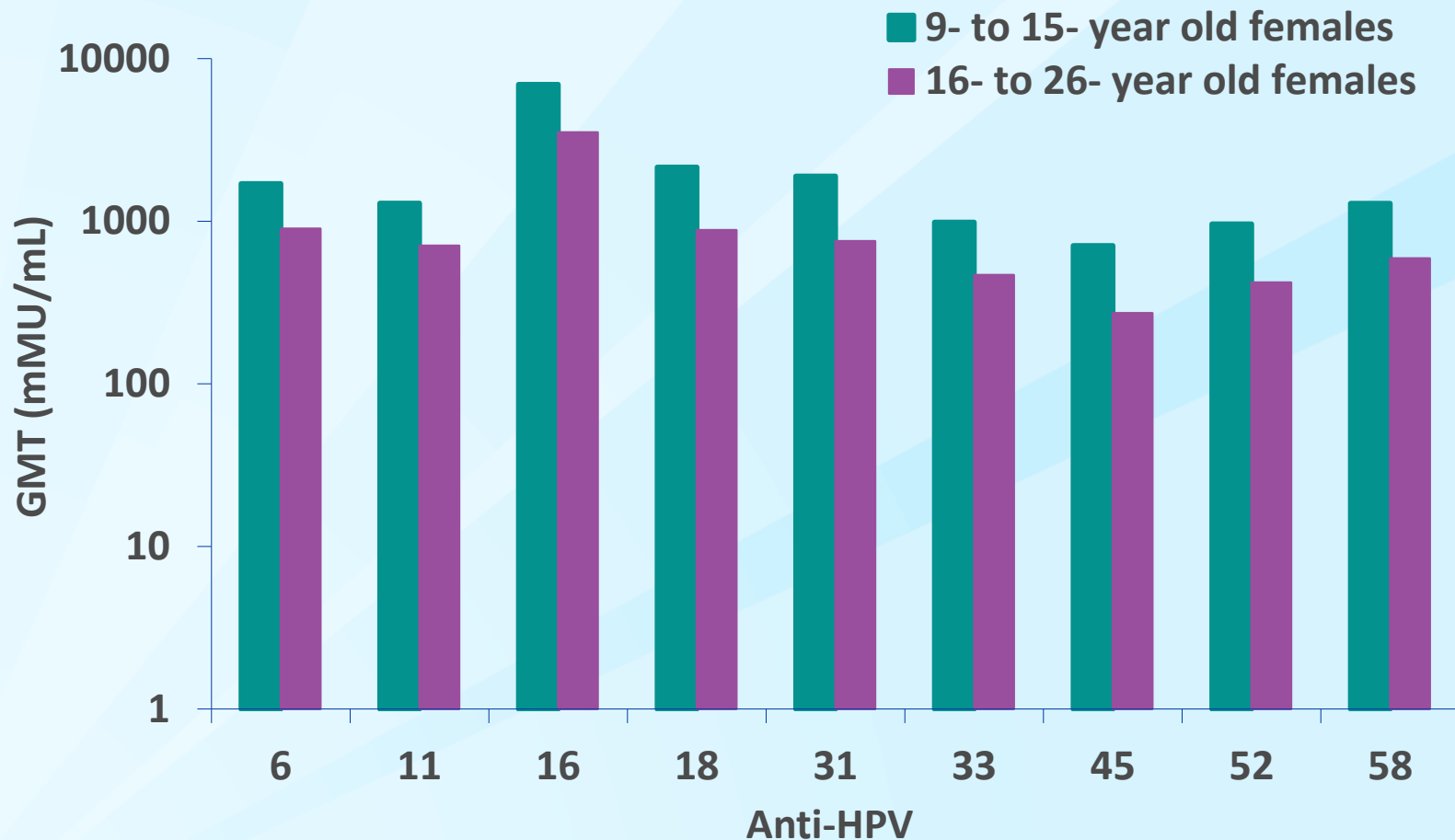
9-valent HPV vaccine efficacy trial per protocol population results

HPV 6,11,16,18 related outcomes	9vHPV n/total	4vHPV n/total
≥CIN2, VIN2/3, VaIN2/3	1/5883	3/5898

- Few high grade outcomes due to HPV 6,11,16,18
- Non-inferiority immunogenicity for HPV 6,11,16,18
 - ≥99% seroconversion; GMTs non-inferior

≥CIN2 = cervical intraepithelial neoplasia grade 2 or 3, or adenocarcinoma in situ; VIN = vulvar intraepithelial neoplasia; VaIN = vaginal intraepithelial neoplasia

9-valent HPV vaccine adult-to-adolescent immunobridging trial



Data from per protocol population; Antibody measured by cLIA at month 7

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM426457.pdf>

9-valent HPV vaccine trials

❑ Efficacy

- ~97% protection against HPV 31,33,45,52,58-related outcomes
- Similar protection against HPV 6,11,16,18-related disease

❑ Non-inferior immunogenicity

- For HPV 6,11,16,18 compared with 4vHPV in 16–26 and 9–15 year olds
- For all 9 HPV vaccine types in adolescent females and males compared to adult females and in adult males compared to adult females

❑ Concomitant use

- No impact on immunogenicity or safety administered concomitantly with quadrivalent meningococcal conjugate vaccine (Menactra) and tetanus, diphtheria, acellular pertussis vaccine (Adacel)

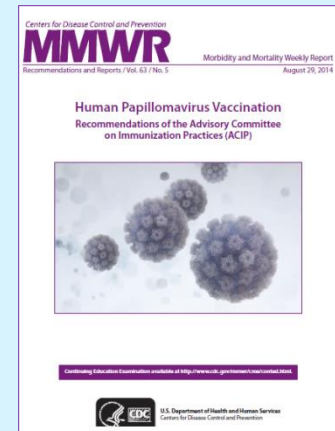
9-valent HPV vaccine safety

- ❑ **Trials included >15,000 9vHPV vaccinees**
- ❑ **Generally well tolerated; safety profile similar to 4vHPV**
 - 9vHPV - more injection-site reactions
 - swelling (40.3% vs 29.1%)
 - erythema (34.0% vs 25.8%)
 - Injection-site erythema and swelling increased with number of doses
- ❑ **Concomitant use**
 - No difference in safety profile when co-administered with quadrivalent meningococcal conjugate vaccine (Menactra) and tetanus, diphtheria, acellular pertussis vaccine (Adacel)

RECOMMENDATIONS

Recommendations for HPV vaccination in the United States (before February 2015)

- ❑ Routine vaccination at age 11 or 12 years*
- ❑ Vaccination recommended through age 26 for females and through age 21 for males not previously vaccinated
- ❑ Vaccination recommended for immunocompromised persons (including persons HIV-infected) and for men who have sex with men through age 26
- ❑ 3-dose schedule (0,1-2 and 6 months)
- ❑ Vaccines
 - 2vHPV or 4vHPV for females
 - 4vHPV for males



*vaccination series can be started at age 9 years

Available HPV vaccines

	Bivalent (Cervarix)	Quadrivalent (Gardasil)	9-valent (Gardasil 9)
Licensed for	Females 9-25 years	Females 9-26 years Males 9-26 years	Females 9-26 years Males 9-15 years

- At the time of the first 9vHPV application to FDA, trials in males 16-26 years had not been completed
- Immunogenicity data now are available for males 16-26 years, reviewed by ACIP and submitted to FDA
- ACIP recommended use of 9vHPV in the currently recommended age groups

Updated ACIP recommendations

- ❑ Routine vaccination at age 11 or 12 years*
- ❑ Vaccination recommended through age 26 for females and through age 21 for males not previously vaccinated
- ❑ Vaccination recommended for men who have sex with men and immunocompromised men (including persons HIV-infected) through age 26
- ❑ Vaccination of females is recommended with 2vHPV, 4vHPV (as long as this formulation is available), or 9vHPV
- ❑ Vaccination of males is recommended with 4vHPV (as long as this formulation is available) or 9vHPV

*vaccination series can be started at 9 years of age

Updated ACIP recommendations

2vHPV, 4vHPV and 9vHPV all protect against HPV 16 and 18, types that cause about 66% of cervical cancers and the majority of other HPV-attributable cancers in the United States. 9vHPV targets five additional cancer causing types, which account for about 15% of cervical cancers. 4vHPV and 9vHPV also protect against HPV 6 and 11, types that cause genital warts.

Updated ACIP recommendations: Interchangeability

If vaccination providers do not know or do not have available the HPV vaccine product previously administered, or are in settings transitioning to 9vHPV, for protection against HPV 16 and 18, any HPV vaccine product may be used to continue or complete the series for females; 4vHPV or 9vHPV may be used to continue or complete the series for males.

Updated ACIP recommendations: Administration

- ❑ 2vHPV, 4vHPV and 9vHPV are each administered in a 3-dose schedule
- ❑ The second dose is administered at least 1 to 2 months after the first dose, and the third dose at least 6 months after the first dose
- ❑ If the vaccine schedule is interrupted, the vaccination series does not need to be restarted

Updated ACIP recommendations: HPV vaccination during pregnancy

- ❑ No change in recommendations
- ❑ HPV vaccine not recommended for use in pregnancy

A new vaccine in pregnancy registry has been established for 9vHPV. Registries for 4vHPV and 2vHPV have been closed with concurrence from FDA.

4vHPV registry closed in 2012

2vHPV registry closed in 2015 <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm434787.htm>

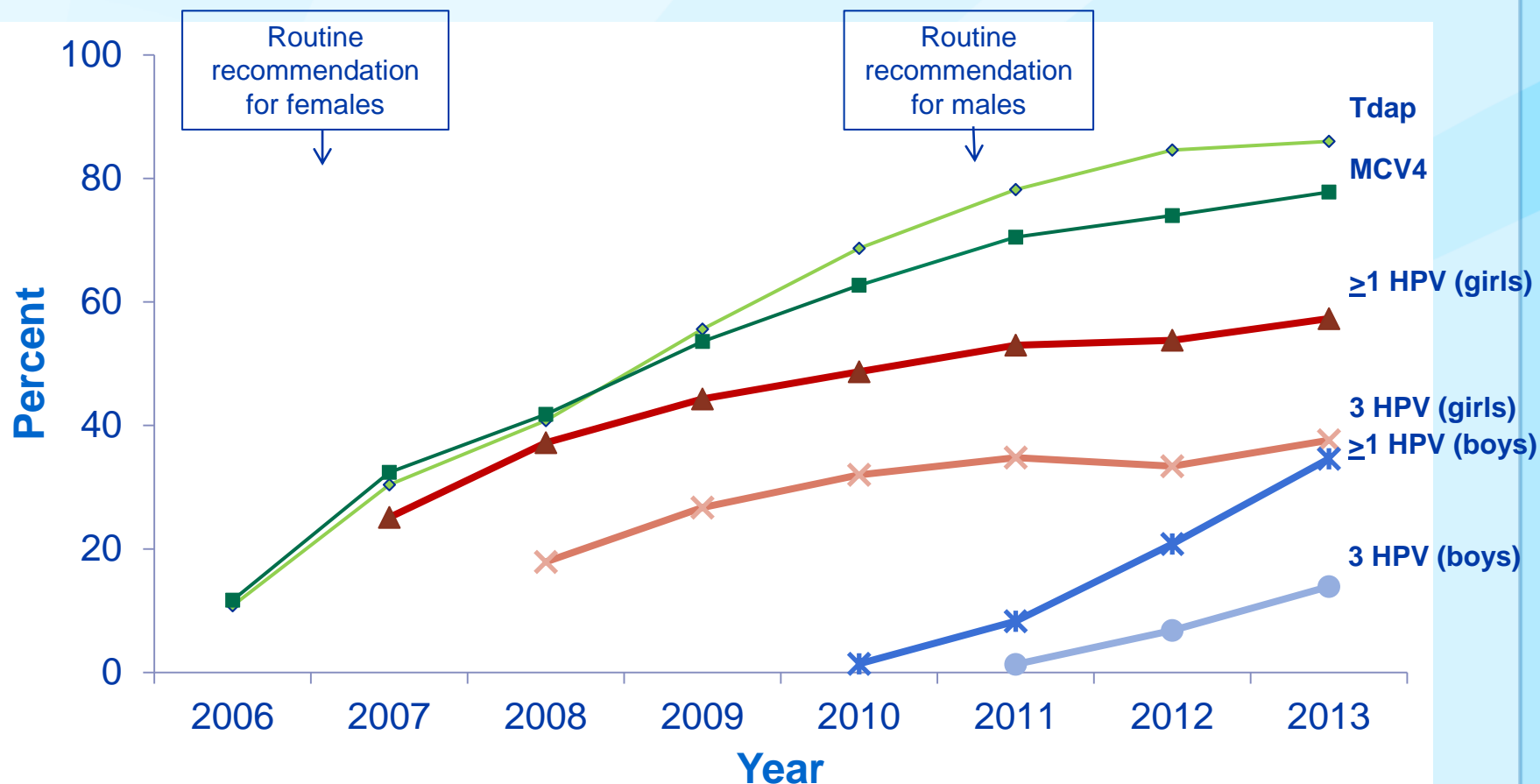
9vHPV vaccination for persons who completed a HPV vaccination series

- ❑ The manufacturer did not seek an indication for 9vHPV vaccination for persons who previously completed a HPV vaccination series
- ❑ A study of 9vHPV in prior 4vHPV vaccinees was conducted
- ❑ Due time limitations (abbreviated ACIP meeting), this was not discussed; will be discussed at a future ACIP meeting

Summary: 9-valent HPV vaccine

- ❑ Licensed by FDA in December 2014
- ❑ Available from manufacturer beginning February 2015
- ❑ Recommended by ACIP in February 2015
- ❑ One of 3 HPV vaccines that can be used for routine vaccination of females and one of 2 for males
- ❑ Targets 5 additional high risk types
 - Overall 14% of HPV-associated cancers in females; 4% in males attributable to these 5 types
 - 15% of cervical cancers attributable to these 5 types
- ❑ CDC awarded a Vaccines for Children (VFC) contract
- ❑ Efforts needed to increase coverage

National estimated vaccination coverage levels among adolescents 13-17 years NIS-Teen, 2006-2013



NIS-Teen = National Immunization Survey-Teen
MMWR 2014;63:625-33

Resources

ACIP website with slides, minutes and recommendations

<http://www.cdc.gov/vaccines/acip/index.html>

Additional resources for providers/patients/clients

<http://www.cdc.gov/vaccines/vpd-vac/hpv/>

www.cdc.gov/vaccines/YouAreTheKey

www.cdc.gov/hpvwww.cdc.gov/vaccines/teens

Thank you

bse4@cdc.gov

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov Web: <http://www.cdc.gov>

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.